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Measurement of Direct Oral Anticoagulants Levels in Patients Admitted for Bleeding Events

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Published in:
Research and practice in thrombosis and haemostasis

Publication date:
2017

Document Version
Publisher's PDF, also known as Version of record

[Link to publication](#)

Citation for pulished version (HARVARD):
Sennesael, A-L, Larock, A-S, Douxfils, J, Dogne, J-M, Spinewine, A & Mullier, F 2017, Measurement of Direct Oral Anticoagulants Levels in Patients Admitted for Bleeding Events: A Prospective Study. in Research and practice in thrombosis and haemostasis: Abstracts of the XXVI Congress of the International Society on Thrombosis and Haemostasis, July 8–13, 2017. pp. 989, XXVI Congress of the International Society on Thrombosis and Haemostasis, Berlin, Germany, 8/07/17.

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TABLE 1 Patient characteristics, management of bleeding and biological measurements for major bleeding events

Gender, age (years)	CLcr (ml/min)	DOAC (dosage, indication)	Time after last intake (hours)	Site of bleeding	DOAC plasma concentrations (ng/ml)	Management	Length of stay (days)	Outcome at 90 days
F, 70	Unknown	Rivaroxaban 15 mg OD, SPAF	22	GI bleeding	Biophen DiXal: 237.5	RBC (3 units)*	Unknown	Unknown
F, 87	48	Rivaroxaban 20 mg OD, VTE	38	GI bleeding	Biophen DiXal: 70.8	RBC (2 units)*	3	Alive
F, 67	53	Rivaroxaban 20 mg OD, SPAF	27	GI bleeding	Biophen DiXal Low: 58.3	RBC (3 units)*	1	Alive
F, 74	73	Apixaban 5 mg BID, SPAF	5	IC bleeding	Biophen DiXal: 298.0	-	9	Alive
F, 77	61	Rivaroxaban 15 mg OD, SPAF	27	IC bleeding	Biophen DiXal: 139.4	PCC 2500 IU (40 IU/kg)	43	Alive
F, 76	33	Dabigatran etexilate 110 mg BID, SPAF	53	GI bleeding	HTI Low: 19.0	RBC (1 unit)	34	Alive
F, 90	60	Rivaroxaban 15 mg OD, SPAF	27	IC bleeding	Biophen DiXal: 86.5	-	1	Alive

* Transfusion before blood sampling. BID: twice daily, CLcr: creatinine clearance (according to Cockcroft-Gault equation), Biophen DiXal: Biophen® Direct Factor Xa Inhibitors, GI: gastrointestinal, HTI: Hemoclot Thrombin Inhibitor®, IC: intracranial, OD: once daily, PCC: prothrombin complex concentrates, RBC: red blood cells, SPAF: stroke prevention in atrial fibrillation, VTE: venous thromboembolism

the ROTEM®; Clotting Time (CT), Clot Formation Time (CFT), α -angle, Maximum Clot Firmness (MCF) were analyzed.

Results: Rivaroxaban and dabigatran, prolonged the CT but did not significantly alter the CFT, the α -angle and the MCF. At equivalent gravimetric concentrations dabigatran effect was more pronounced compared to rivaroxaban. When the two agents were combined no amplificatory effect on CT was observed. The α -angle and MCF were not significantly affected. Tinzaparin induced a significant prolongation of CT and CFT and reduced the α -angle and MCF values as compared to the control. Tinzaparin impact was significantly more potent than the DOAC combination used even at the higher studied concentrations.

Conclusions: When coagulation is triggered by physiologically relevant concentrations of TF, rivaroxaban and dabigatran prolong the CT, did not alter fibrin polymerization kinetics nor clot firmness. The combination of rivaroxaban and dabigatran did not alter clot formation process suggesting that the important effect of tinzaparin on clot formation quality is not linked to its anti-Xa or anti-IIa activity association but most probably is related to a direct interference with fibrin network and others antithrombin dependent inhibitory effects.

PB 1240 | Measurement of Direct Oral Anticoagulants Levels in Patients Admitted for Bleeding Events: A Prospective Study

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Background: Although direct oral anticoagulants (DOAC) do not require close laboratory monitoring, their measurement remains useful in specific clinical situations. A therapeutic range has not been defined yet, but DOAC plasma concentrations were shown to correlate with bleeding outcomes.

Aims: To describe DOAC plasma concentrations in patients with bleeding events, in relation to clinical and medication data.

Methods: As part of a prospective observational study conducted in the emergency departments of 2 hospitals, we collected 14 plasma samples from DOAC-treated patients admitted for bleeding events. Routine clotting assays were performed as well as specific assays using CE approved procedures (calibrated chromogenic anti-Xa assays for apixaban and rivaroxaban and diluted thrombin time and ecarin chromogenic assay for dabigatran). Clinical data were collected on admission, at discharge and at 90 days. Bleeding severity was assessed using ISTH definition. The study was approved by the Ethics Committees.

Results: Patients (median age 75 years) were mainly treated with rivaroxaban (10/14), for stroke prevention in atrial fibrillation (10/14). The most frequent site of bleeding was gastrointestinal (6/14). Seven bleedings were major (table 1).

Conclusions: A large range of DOAC plasma concentrations was observed, with above on-therapy levels estimated in around half of patients admitted for bleeding events. Among the factors contributing to bleeding, potential drug interactions are frequent in anticoagulated patients and should be screened.